

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference PR60538WO	FOR FURTHER ACTION		See item 4 below
International application No. PCT/US2004/033585	International filing date (<i>day/month/year</i>) 12 October 2004 (12.10.2004)	Priority date (<i>day/month/year</i>) 16 October 2003 (16.10.2003)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant SMITHKLINE BEECHAM CORPORATION			

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | |
|-------------------------------------|---|
| <input checked="" type="checkbox"/> | Box No. I Basis of the report |
| <input type="checkbox"/> | Box No. II Priority |
| <input type="checkbox"/> | Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input checked="" type="checkbox"/> | Box No. VI Certain documents cited |
| <input checked="" type="checkbox"/> | Box No. VII Certain defects in the international application |
| <input checked="" type="checkbox"/> | Box No. VIII Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

Date of issuance of this report 18 April 2006 (18.04.2006)

Authorized officer

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Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

28/4

REC'D 24 MAR 2005

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION

See paragraph 2 below

International application No.
PCT/US2004/033585

International filing date (day/month/year)
12.10.2004

Priority date (day/month/year)
16.10.2003

International Patent Classification (IPC) or both national classification and IPC
C07D409/04

Applicant
SMITHKLINE BEECHAM CORPORATION

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/033585

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - a sequence listing
 - table(s) related to the sequence listing
 - b. format of material:
 - in written format
 - in computer readable form
 - c. time of filing/furnishing:
 - contained in the international application as filed.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority for the purposes of search.
3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/033585

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N) Yes: Claims 2-4,6-8
 No: Claims 1,5

Inventive step (IS) Yes: Claims
 No: Claims 1-8

Industrial applicability (IA) Yes: Claims 1-8
 No: Claims

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

V and VI

Reference is made to the following documents:

- D1: DESAI, J AND SHAH V.H.: "Reactions of Methyl 3-Hydroxythiophene-2-carboxylate. Part 4. Synthesis of Methyl 5-Azolyl-3-hydroxythiophene-2-carboxylates" JOURNAL OF HETEROCYCLIC CHEMISTRY, vol. 24, 1987, pages 1301-1303, XP002320501
- D2: US-A-5 990 146 (BOSCHELLI ET AL) 23 November 1999 (1999-11-23)
- D3: BRIAN D. PALMER ET AL.: "Structure-Activity Relationships for 1-Phenylbenzimidazoles as selective ATP Site Inhibitors of the Platelet-Derived Growth Factor Receptor" JOURNAL OF MEDICINAL CHEMISTRY, vol. 41, 1998, pages 5457-5465, XP002320502
- D4: WO 2004/014899 A (SMITHKLINE BEECHAM CORPORATION; ANDREWS, III, CLARENCE, W; CHEUNG, MUI) 19 February 2004 (2004-02-19)

Novelty

The following disclosures from D1 are novelty destroying to the present claim 1 and 5:

Scheme 2 of D1 together with the disclosure of the product in the table, wherein X is hydrogen and the azolyl is benzimidazolyl.

Experiment 1, method a. together with the product wherein X is hydrogen and azolyl is benzimidazolyl

It may be noted that the benzimidazolyl can be regarded as both a reactant, but also as a base additive.

D2 and D3 do not disclose the direct reaction of a thiophen compound with a benzimidazole compound.

Inventive Step

D1 is considered to be the closest prior art.

In view of the disclosures of D1, which anticipate the present claim 1, the skilled person would have arrived at the present claims.

The problem underlying the present application is considered to be the provision of a process having surprising effects compared to that of D1.

In the absence for evidence for such a surprising effect an inventive step cannot be acknowledged.

It may be noted that the surprisng effect should be connected with the distinguishing feature of the invention.

VI

For the purposes of this communication it has been assumed that the priority of the present application is valid.

D4 does not constitute prior art within the meaning of Rule 64.1 (b).

The filing date of D4 is earlier than the priority date of the present application.

VII

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D3 is not mentioned in the description, nor are these document/s identified therein.

VIII

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2004/033585

The term "physiologically functional derivative" indicated in claim 14 leads to an unclear scope of claim, since it is unclear which structures are intended.

The term "derivative" includes compounds obtained from another compound by a chemical reaction and therefore derivatives of pilocarpine or pilopoic acid ring open forms of pilocarpine or pilopic acid, structures which are structurally remote from the starting material, functional derivatives, compounds wherein the heteroatoms are exchanged by alternative atoms, compounds with numerous different types of side groups etc.